PROGRESS

OF

MEDICAL SCIENCE.

THERAPEUTICS.

UNDER THE CHARGE OF

FRANCIS H. WILLIAMS, M.D.,
ASSISTANT PROFESSOR OF THERAPEUTICS IN HARVARD UNIVERSITY.

SPARTEINE.

A careful comparative study of the action and uses of some members of the group of cardiac drugs has recently been made by PROFESSOR LEWASCHEW, and the result of his work deserves attention.

Since the introduction of digitalis, about a century ago, the means at our command for the treatment of cardiac diseases have been steadily increasing in number. As a rule, each drug of the class of cardiac tonics has a more marked action on the heart when first given than after its administration has been kept up for some time; if, however, another member of this class be substituted for the first, the substitute may be able to exert its full power. In long-continued treatment one is obliged, therefore, to change the drug from time to time, and for this reason the discovery of new remedies which have a similar action contributes to lengthen the life of the patient, especially in the period in which compensation is accomplished only with the assistance of cardiac remedies. Further, while these remedies may, in the main, have a similar influence on the heart, some have a marked action on the nervous system, others on some special organ; and it is not a matter of indifference which of these means one chooses for various patients, or even for different stages of the disease in the same patient.

Therefore every increase of our resources is desirable and to be welcomed as an enrichment of the resources at our command, and is not to be looked upon as the result of a hunt after novelties, or as throwing discredit and distrust upon digitalis. Each drug should be carefully studied that we may learn how far it is capable of acting as a substitute for digitalis, adonis, etc., and what the accompaniments of such action may be.

Sparteine has been studied by many observers, and a review of the labors of those who have cultivated the field, experimentally and clinically, shows a wide divergence of opinion. Germain Seé, Laborde, and Legris ascribe to sparteine an action on the heart as energetic or even more active than that exerted by digitalis. On the other hand, Fronmüller noted an increase in the amount of urine excreted, but does not mention its action on the heart. Leo also noted diuresis, which he ascribes to an action of sparteine directly upon the renal epithelium. H. Voigt, Stoessel, and Prior recognized the action of sparteine upon the heart, but considered it much less in degree than occurs with digitalis. They also noted an increase in the amount of urine, but ascribed it to the influence of sparteine on the circulation.

Finally, Nasius denies to sparteine any action on the heart or urine.

Such differences of opinion about the action of sparteine are extended also to what should constitute the proper dose. Authors give amounts varying from three grains several times a day to one-thirtieth or one-sixtieth of a grain at a dose, with one-fifteenth of a grain as a daily maximum.

Professor Lewaschew's aim was not only to find out whether sparteine does act upon the heart, and if so in what manner, but also to determine if it causes diuresis, and if so, in what manner it is accomplished. Further, to ascertain if sparteine is of any therapeutic service in cardiac diseases, and especially to study the relation between sparteine and other drugs acting upon the heart and kidneys.

Sparteine was given in 22 cases of cardiac disease, and in only 7 was there any obvious therapeutic action. Of the 15 others, 3 were not relieved by large or small doses of sparteine nor by digitalis or adonis; 12 of the 15, though not relieved by any of a variety of doses of sparteine, did respond to medium and large doses of adonis and digitalis by stronger and more regular cardiac action, increase in the amount of urine, diminution and disappearance of the œdema, relief of the embarrassed respiration, etc. A comparison of these 12 cases with the 7 in which sparteine proved serviceable, shows that the 12 cases were in the later and the 7 cases in the earlier stages of failure of compensation, in which even a suitable regime might have afforded relief. In slight disturbances of the heart's function sparteine, as well as a small amount of adonis, digitalis, or strophanthus, is capable of a moderate therapeutic action, but where the changes in the heart are more considerable sparteine is inactive and has to be replaced by remedies whose effect is more vigorous.

In no case was it found that sparteine had any influence to increase or regulate the heart's action, or promote diuresis, when this had not been accomplished by sufficient doses of digitalis, adonis, or strophanthus.

The results obtained by Professor Lewaschew explain the discrepancies of the observers who have reported upon the action of this drug, those who noted a marked therapeutic action from the drug probably used it in cases where the failure of compensation was slight, and, on the other hand, the authors who condemned sparteine probably gave it in old cases where there was much degeneration of the cardiac muscle and the conditions such as to lead them to infer that the drug had little or no influence in cardiac disease.

It does not seem probable, in view of the experience in the seven cases where sparteine was given with success, that it will prove of lasting service in any patient. Among these seven cases, in which sparteine was more or less successful, there was only one in which it succeeded in restoring the balance of the circulation for any considerable period, in all the other cases it was necessary to resort to adonis, digitalis, or strophanthus.

As regards other action of sparteine than that of the heart. It relieved the breathing and asthma, at the same time it increased more or less the amount of urine, whether this last was brought about, as some believe, through the circulation, or, as others assert, through the renal epithelium, is not easily proven by clinical observation. It is more probable that it is the result of improvement in the circulation. In the cases in which sparteine had a diuretic action it also increased the heart's action as well and made it more regular; on the other hand, there was never any diuresis without cardiac stimulation, though it did not occur in all cases in which the heart was influenced by the drug. Further, if sparteine is a diuretic through action on the kidneys and independently of the circulation it should increase the flow of urine in diseases, like cirrhosis of the liver, where the dropsy is not dependent upon a weak heart; but in these cases all observers agree that it does not increase the urine or diminish the œdema. In health the drug does not seem to have any marked influence on the amount of urine secreted.

The rapidity with which the action of this drug may be induced deserves attention; and here also the views of different observers are not in accord. In the cases where positive results followed the administration of sparteine a series of observations on the heart and blood-pressure were made both before and after its administration; it was ascertained that the action of sparteine when it took place at all, appeared promptly, in some cases it began in fifteen minutes after it had been taken.

In general, it may be said that sparteine is capable of strengthening and regulating a weak and irregular heart, and that this action is exerted promptly, though it is far weaker than that of digitalis, adonis, and strophanthus. It promotes diuresis in cardiac cases, and this action cannot be said to be the result of a local action on the kidneys.

The dose is from one and a half to four and a half grains a day, given in three or four doses. In these amounts the undesirable accompaniments do not go beyond irritation of the alimentary canal, which may result in diarrhœa, seldom in nausea and vomiting.[1]

A CONTRIBUTION TO OUR KNOWLEDGE OF THE PHYSIOLOGICAL ACTION OF ANTIPYRIN.

RAYNER D. BATTEN and T. J. BOKENHAM took up the subject of the physiological action of antipyrin in order to find out in what manner the drug might act in megrim and kindred diseases. The experiments were conducted in the laboratory of Dr. Brunton, and the experimenters had the benefit of his advice and suggestions.

These investigators conclude that the main, if not the sole, action of antipyrin is due directly or indirectly to its influence on the nervous system. It appears to act on all parts of it, mainly on the spinal cord, but also on the brain and motor nerves. Means of absolutely satisfying themselves as to the tracts of the spinal cord which are specially affected by antipyrin were not found, but if the symptoms produced by a drug may be compared with those the result of a disease, the localization of antipyrin is fairly obvious. The symptoms in question bear a very strong resemblance to those of lateral sclerosis, and they, therefore, think that the action of the drug may be localized in the lateral columns of the cord. For instance, in guinea-pigs and a cat spastic rigidity of the hind limbs was found, and, in all animals experimented upon, rigidity formed a marked symptom. Further, in the first-mentioned animals this symptom appeared to come on with any attempt to use the limbs, just as is the case with a patient with lateral sclerosis.

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[1] Zeitschrift für klinische Medicin, vol. xvi., 1889.

The excess of myotatic irritability is also very marked, the slightest tap being sufficient to evoke violent muscular contractions, and in extreme cases to cause clonic spasms of the whole body. In one experiment phenomena exactly similar to those of ankle-clonus were obtained. In all cases the contrast between the effect of painful stimuli and stimuli such as the slightest taps, or even the vibrations produced by walking about the room, was most marked, the former producing less effect than in a normal animal, while the latter caused the violent spasmodic movements already mentioned.

The localization of the action of drugs on the different tracts of the spinal cord appears to be a field of research in which, as yet, little has been done, and is one that gives promise of very interesting and useful results. The effects of antipyrin are so transient, seldom extending over more than a few hours, and the recovery is so complete that pathological results demonstrable by the microscope are hardly to be expected. Further, doses sufficient to cause death produce other symptoms not referable to the lateral columns alone.

The importance of being able to localize the action of a drug to a special tract of tissue cannot be over-estimated, and if further work should prove this to be possible it will go far to render the use of drugs in diseases of the nervous system a more rational proceeding. As regards the action of antipyrin on the brain of mammals, but little can be said at present. From the rapid rhythmic movements noticed in many cases, and from the circuo-movements sometimes observed, it may be concluded that either the motor centres themselves are involved, or that their inhibitory power is abolished.

Clinically, we sometimes meet with cases of poisoning by antipyrin, and it is interesting to observe that here, also, the symptoms are mainly nervous.—*British Medical Journal*, June 1, 1889.

INTOLERANCE OF ANTIPYRIN.

In view of the frequent use of antipyrin, both with and without the advice of a physician, and in connection with the physiological action of this drug, the following case is suggestive:

In a man of fifty years, suffering from sciatica, five grains of antipyrin three times a day were prescribed. The first and only dose was taken at 11.30 A. M. He instantly experienced a sensation of tingling and burning in his gums, which rapidly extended to the throat and nose, accompanied by sneezing, running from the eyes and nostrils, dizziness, complete loss of vision, a feeling of numberless pins pricking him down each side of the neck, tightness in the throat, and dyspnœa.

The pin-pricking sensation extended rapidly down the right side of his chest and abdomen, and was particularly severe in the right side of the scrotum and right testicle, and was also felt in the legs and feet—severely in the right and slightly in the left.

He next experienced a sensation as if the contents of his thorax and abdomen were being forcibly drawn upward toward his throat, and the right testicle toward the abdomen; so that, he says, he "was drawn in a ruck," and, being no longer able to stand, he fell on the floor. He trembled violently all over, and had a cramp in his right arm and hand.

His physician arrived fifteen minutes after he had taken the dose, and found him sitting in a chair declaring that he was unable to remain in a recumbent posture. His face was of a dusky red color; his nose, lips, and eyelids were so swollen as to render his features quite unrecognizable; he was trembling violently all over, and the fingers of his right hand were clenched in the form of a claw. Pulse scarcely perceptible.

The symptoms gradually subsided; the following day, with the exception of a slight headache and loss of appetite, he had completely recovered.—*British Medical Journal*, June 15, 1889.

Antipyrin in the Treatment of Hæmorrhoidal Ulcers.

Dr. J. Schreiber gives an account of a man, seventy-two years old, who had suffered for ten years with the most obstinate hæmorrhoidal ulcers. By dusting the ulcers for twenty days with finely powdered antipyrin he produced a perfect cure. Each application caused moderate pain, lasting about half a minute, but the effect of the drug on the pain and continual itching of the ulcers was very favorable.—*New York Medical Journal*, May 11, 1889.

Antipyrin in Diabetes Mellitus.

For some time past the attention of several well-known French physicians has been given to the treatment of glycosuria with antipyrin, the results obtained being such as to merit a very favorable opinion of its value in such cases. One of those who have reported on it at length is M. Germain Sée, who, while administering antipyrin to a diabetic patient for neuralgia, was astonished to find that the sugar entirely disappeared from the urine. Previous to this, however, Huchard had used it with good effect in polyuria, and Dujardin-Beaumetz in diabetes. Germain Sée, having confirmed his first observation, made a series of experiments on animals in which he had induced glycosuria artificially, and these further demonstrated the power of the drug to diminish the excretion of glucose. He is an upholder of the theory that in diabetes there is an over-production of glucose, and maintains that consequently the prime indications are—(1) to use drugs which depress the nervous system, and thereby lessen the chemical and nutritive activity of the body, and (2) to reduce the sources of glucose by giving chiefly a flesh and fat diet.

The first indication is met by antipyrin, which has in a remarkable degree the power of depressing the excitability of the central nervous system, and at the same time of lessening the excretion of urinary solids and water. Hence there can be no doubt that the entire bodily metabolism is retarded by it. In this country opium and its derivatives are the drugs chiefly relied on for the treatment of diabetes, and it is pretty generally recognized that their beneficial effects are due to the similar sedative action which they exert on the activity of the nervous system. The second indication is met, of course, by the classical dietetic treatment.

Sée has observed carefully eighteen cases, in five of which the prognosis, owing to tubercle or rapid emaciation, was hopeless from the beginning. The other thirteen were typical cases of diabetes mellitus, passing two to six litres of urine per diem, containing twenty-five to eighty-five grammes of glucose per litre. All these improved rapidly in from three to twenty days, the urgent symptoms passing off, and the sugar falling to a few grammes, or entirely disappearing. Various complications, such as boils, eczema, pruritus, and neuralgia, disappeared at the same time. All these patients suffered more or less from obesity, a diminution in which was often one of the first signs of recovery. As soon as the increased appetite and the exaggerated formation of glycogenic material are stopped, the obesity, which is the consequence of the transformation of much of the food into fat, begins rapidly to diminish. The best results are obtained by the administration daily of 48 grains of antipyrin, in three doses. Sée is strongly of opinion that the dietary should contain about seven ounces of fresh bread, and the same quantity of boiled potatoes, in the twenty-four hours. This, he points out, satisfies the craving of the patient for carbohydrates, and has a good effect on his general health, while both articles of food, owing to the large percentage of water which they contain, really convey less starch to the patient than the toasted bread or dried crusts which are so often allowed.

Robin has also recorded very carefully the observations made by him in four cases of diabetes, all occurring in patients well past middle life. His results, however, cannot be said to be more encouraging than those which we already obtain by combining a dietetic treatment with large doses of opium. He is of opinion that although antipyrin does not cure glycosuria, it nevertheless exercises so decided and energetic an effect on the excretion of glucose, and such an improvement in the various symptoms, that it is worthy of an extended trial. He gives various cautions regarding it, pointing out that larger doses than 48 grains per diem are apt to cause slight albuminuria, while one frequently sees loss of appetite, pallor, puffiness of eyelids, or a feeling of tension in the face, all of which are indications for discontinuing the administration of the drug. It also increases greatly the acidity of the urine, and hence it is advisable to administer bicarbonate of soda along with it. Lastly, he advises that its continuous use should not be prolonged beyond twelve days, an interval of several days being allowed before it is resumed again, and suggests that, by alternating the dietetic and antipyrin treatments, one can advantageously avoid the monotony of the former and the dangers of the latter.

The results obtained so far seem to show that antipyrin will be found of value chiefly in those cases of diabetes occurring in elderly, well-nourished, stout subjects, in whom the prognosis as regards life is favorable. Such patients often object most strenuously to the restrictions imposed on their eating and drinking, and if by the use of antipyrin we can advantageously relax the strictness of the dietary, it must be admitted that we have gained an important addition to our resources for the treatment of diabetes.—*British Medical Journal*, June 29, 1889.

The Topical Use of Acetanilide.

Dr. A. H. Newth has used acetanilide as an external application for a few months, and reports favorably of it as an adjunct to other remedies. He has used it in psoriasis, in association with mercurials. He has also employed it in chronic irritable ulcer, erysipelas, urticaria, herpes, and a few other conditions of the skin, where there has been considerable irritation. The strength of these applications has been, for the most part, twenty grains of the drug to an ounce of lanolin or vaseline.—*New York Medical Journal*, May 4, 1889.

A Tonic Formula.

Dr. Austin Flint has prepared a formula in which most of the important inorganic salts of the blood are represented, with an excess of sodium chloride and a small quantity of reduced iron, the various salts, except the sodium chloride, being in about the relative proportion in which they exist in the normal circulating fluid. The preparation is now made in the form of compressed tablets and sugar-coated tablets.

Saline and chalybeate tonic.

℞.—Sodii chloridi (c. p.)	ʒiij.
Potassii chloridi (c. p.)	gr. ix.
Potassii sulph. (c. p.)	gr. vj.
Potassii carb. (Squibb)	gr. iij.
Sodii carb. (c. p.)	gr. xxxvj.
Magnes. carb.	gr. iij.
Calc. phosp. præcip.	ʒss.
Calc. carb.	gr. iij.
Ferri redacti (Merck)	gr. xxvij.
Ferri carb.	gr. iij.—M.

In capsules No. 60.
Sig.—Two capsules daily after eating.

In the great majority of the cases of anæmia, etc., in which iron was strongly indicated, the tonic seemed to act much more promptly and favorably than the chalybeates usually employed. In a certain number of cases in which patients stated that "they could not take iron in any form," the tonic produced no unpleasant effects.—*New York Medical Journal*, May 18, 1885.

The Internal Use of Chloroform.

Chloroform has long been used internally as a symptomatic remedy in flatulence, diarrhœa, neuralgic pains, and cough. It is a substance which is quickly absorbed by the stomach and as quickly passes out of the system by the lungs, skin, and kidneys. Its specific use for serious maladies has rarely been attempted.

Dr. Stepp was led, by the experiments of Salkowski on the disinfecting power of chloroform water, to try its effects in acute pharyngitis, diphtheria, whooping-cough, croupous pneumonia, and typhoid fever. Negative results were obtained in diphtheritic and in tubercular cases, although locally, as a gargle, chloroform water is very useful.

Dr. Stepp particularly insists, however, upon the value of chloroform water in typhoid fever. The mode of application was fifteen drops of chloroform dissolved in five ounces of water given in equal parts daily. The temperature was invariably found to sink in a few days so as to induce reconvalescence.

But far more remarkable was the influence exerted by the chloroform treatment upon the sensory organs. Numbness, the specific typhoid face and expression, and hardness of hearing disappeared under the treatment in three to four days; the patients grew lively and cheerful, and nothing short of an actual measuring of the temperature would have betrayed the presence of the insidious malady. The author ascribes this favorable influence of chloroform over the typhoid process, not to any disinfecting properties of the drug itself, but to the products of its chemical decomposition within the system.—*Medical Record*, June 8, 1889.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D., F.R.C.P. LOND.,
PHYSICIAN-IN-CHIEF OF JOHNS HOPKINS HOSPITAL, BALTIMORE.

ASSISTED BY

J. P. CROZER GRIFFITH, M.D.,
ASSISTANT PHYSICIAN TO THE HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA.

WALTER MENDELSON, M.D.,
OF NEW YORK.

HÆMOGLOBINURIA.

BRISTOWE (*Brit. Med. Journ.*, 1889, 1, 998) has made some clinical experiments on a case of hæmoglobinuria, which are so valuable that they deserve an extended notice. The patient had, in the winter of 1885–6, lost several phalanges by what he said was frost-bite, but which the author thinks had some connection with Reynaud's disease. The following winter, after prolonged exposure to cold, he was seized with shivering and headache, followed by a discharge of porter-colored urine. There was also pain and difficulty in swallowing. Though well each summer, he suffered in a similar way each winter. On admission to the hospital he was pale and sallow. There was no fever. The urine contained hæmoglobin and a little albumin, but on the following day was normal. As these attacks came on the least exposure to cold, it was resolved to make some experiments upon him, with his consent. He was accordingly sent out for a walk lasting three-quarters of an hour. He returned, shivering, bluish, with no appetite, with a sensation of swelling of the throat, with hands livid and swollen, and with feet cold. The temperature was 102° F., and in two hours there was hæmoglobinuria. On the next day the condition was normal. Several similar experiments were made; the symptoms being virtually the same on each occasion. On several occasions the blood was examined, and it was found that each attack was accompanied by decided temporary diminution of the number of red blood-cells, and